The Bioscan 7(3) : 473-475, 2012
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
www.thebioscan.in

HAEMATOLOGICAL CHANGES IN PREGNANT RATS AND THEIR DESCENDANTS DUE TO TERATOGENIC DOSE OF CADMIUM CHLORIDE

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KEY WORDS
Haematology
Teratology
Cadmium Chloride
Rat
Cadmium toxicity

Received on :
12.05.2012

Accepted on :
29.07.2012

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ABSTRACT
The present study was envisaged to evaluate the effect of teratogenic dose of Cadmium Chloride ($CdCl_2$) in pregnant rats as well as their descendants on haematological parameters. Teratogenic dose (15mg of $CdCl_2$/ kg body weight) when given to pregnant rats from day 7 to 15 of gestation has caused a marked elevation in Red blood corpuscles (RBC), Haemoglobin (Hb), packed cell volume (PCV), mean corpuscle haemoglobin concentration (MCHC) and white blood corpuscles (WBC) on day 15 and 20 of gestation period. In contrast we noticed a fall in mean corpuscle volume (MCV) and mean corpuscle haemoglobin (MCH) in dams treated with teratogenic dose of $CdCl_2$. The changes were more prominent on 20th day when compared to 15th day pregnant rats. However no significant change was noticed in the offsprings from these dams, when their blood was checked for the same parameters on day 10th and 30th of their postnatal age. Thus, results of the present study revealed that haematological parameters of maternal blood are quite susceptible to teratogenic dose of $CdCl_2$ than to produce alterations in their offsprings.

INTRODUCTION

In recent years there has been a great concern over heavy metal pollution. Among them, cadmium is highly toxic and one of the most important pollutant. Batteries are the main source of pollution, However, combustion of coal, mineral oil, smelting, mining, alloy processing and many other industries that use cadmium are also potential source of cadmium pollution (Friberg *et al.,* 1976; Swarup *et al.,* 2007). From earlier reports, it is evident that in mammals cadmium at moderate doses appears to produce kidney damage (Bernard, 2004) and hypertension (Schroeder, 1965). It has also been implicated in the causation of ouch-ouch disease in Human beings (Tsuchiya, 1969). In another study Mlynarcikova *et al.* (2005) reported female infertility in humans following exposure to cadmium through cigatette smoke. However, their exists a lacunae regarding its effects on haematological parameters of mammals especially during pregnancy. Hence, an attempt has been made to evaluate the effects of teratogenic dose of $CdCl_2$ in pregnant rats as well as their offsprings.

MATERIALS AND METHODS

Virgin rats (*Rattus nonvergicus*) were procured and maintained in well conditioned animal house for a week and were fed with food and water *ad libitium*. Adult females, weighing 170 ± 10g, in different groups were administered orally with different doses of $CdCl_2$ dissolved in distilled water for 24h. LD_{50} was calculated by probit method (Finney, 1971) and was found to be 270mg/kg. Experiment protocols involving the use of animals were approved by the animal ethics committee. Virgin adult female rats were caged overnight with virgin males. The day, on which a sperm was found in the vaginal smear, was taken as day 1 of pregnancy. Teratogenic dose was evaluated by administering different doses of $CdCl_2$ (0, 2.5, 5, 10, 15, 20 mg/kg) to the above pregnant rats orally from day 7 to 15 of gestation. Since fetuses from dams treated with 15 mg of $CdCl_2$/ kg body weight, showed morphological anomalies like short tail, syndactyly etc., hence this dose was selected as teratogenic dose for the present study. Blood samples were collected on day 15 and 20 of gestation period of control pregnant rats as well as pregnant rats administered with teratogenic dose of $CdCl_2$ from day 7 to day 15 of gestation period. For neonatal studies, blood from 20 and 30days old offsprings of rats treated with teratogenic dose of $CaCl_2$ from day 7 to 15 of gestation was also collected.

Blood was analyzed for the estimation of the RBC count (Davidson and Henry, 1969) the haemoglobin (Sahli, 1966) and packed cell volume (PCV) (Schalm *et al.,* 1975). From this the mean corpuscular volume (MCV), The mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated. The results were subjected to student's ' t' test for statistical significance (Pillai and Sinha, 1978).

RESULTS AND DISCUSSION

In pregnant rats, teratogenic dose of $CdCl_2$ has produced

Table 1: Changes in hematological parameters at different gestation times of rats given teratogenic dose of $CdCl_2$ from day 7 to day 15 of gestation

Parameter	15 days Control	Expt.	20 days Control	Expt.
RBC (millions/Cu mm)	8.46 ± 0.32	11.24 ± 0.81(+32.86)	8.22 ± 0.24	11.48 ± 1.02(+39.66)
Hb (g/100 mL)	13.86 ± 0.92	20.67 ± 1.21(+49.35)	13.17 ± 0.102	20.21 ± 1.28(+53.45)
PCV (%)	46.27 ± 4.10	55.36 ± 3.7(+19.65)	47.92 ± 2.27	58.41 ± 4.62(+21.89)
MCV (C.u)	54.69 ± 4.32	49.25 ± 4.78(-9.95)	58.30 ± 3.23	46.56 ± 2.67(-20.14)
MCH(u.ug)	16.36 ± 1.13	18.39 ± 0.98(+12.41)	16.02 ± 1.08	17.60 ± 1.13(+9.86)
MCHC(%)	29.91 ± 0.292	37.34 ± 2.16(+24.84)	27.48 ± 1.282	34.60 ± 2.82(+25.91)
WBC (thousands/Cu mm)	6.92 ± 0.26	8.84 ± 0.71(+27.75)	7.06 ± 0.72	9.12 ± 0.82(+29.18)

Values are Mean ± SD of six individual observations; Values in parentheses are percent change from control; Values are significant at $p < 0.05$

Table 2: Changes in hematological parameters in litters following administration of rats with teratogenic dose of $CdCl_2$ from day 7 to day 15 of gestation

Parameter	10 days Control	Expt.	30 days Control	Expt.
RBC (millions/Cu mm)	9.32 ± 0.41	9.64 ± 0.37(+3.43)	9.82 ± 0.22	9.12 ± 0.17(-7.13)
Hb (g/100mL)	12.27 ± 0.90	12.39 ± 0.72(+9.78)	12.92 ± 0.69	13.21 ± 1.01(+2.25)
PCV (%)	48.77 ± 3.21	50.21 ± 4.09(+4.00)	47.38 ± 3.27	49.04 ± 3.09(+3.51)
MCV (C.u)	52.33 ± 2.44	52.09 ± 1.19(-0.50)	48.25 ± 3.37	53.77* ± 2.98(+11.44)
MCH(u.ug)	13.16 ± 0.82	12.85 ± 0.72(-2.36)	13.16 ± 0.60	14.49* ± 1.02(+10.11)
MCHC(%)	25.16 ± 1.19	24.67 ± 1.43(-1.95)	27.27 ± 2.01	26.94 ± 0.98(-1.21)
WBC (thousands/Cu mm)	5.07 ± 0.31	5.62* ± 0.23(+10.85)	5.71 ± 0.18	6.33* ± 0.22(+10.85)

Values are Mean ± SD of six individual observations; Values in parentheses are percent change from control; *Values are significant at $p < 0.05$; Changes are insignificant

marked elevation in RBC count, haemoglobin (Hb) concentration, packed cell volume (PCV) and WBC on day 15 and 20 of gestation period (Table 1). MCHC was also fairly increased but a fall in MCV was observed in the values of various parameters when it was compared with the controls. Contrary to this there were no significant changes in the haematological parameters in litters of 20 and 30 days old when compared to that of controls (Table 2).

The probable reason for the increase in RBC count and haemoglobin concentration in pregnant rats administered with teratogenic dose of $CdCl_2$ could be due to prevailing hypoxic conditions in the animals. It has also been reported that dehydration or loss of fluid from circulation could also contribute to increase in RBC count (Bansal *et al.,* 1979). It has also been established that erythropoietic stimulating factor (ESF) in the plasma of animals directly acts on bone marrow during the periods of low oxygen tension and stimulates RBC production (Van Liere and Stistiney, 1963). So the present study, obviously suggests that the $CaCl_2$ intoxicated rats appear to cope with the adverse conditions by increasing their respiratory capability through elevated RBC and Hb Synthesis.

The teratogenic dose of $CdCl_2$ increased the PVC of blood of pregnant rats. This appears reasonable since it is known that PVC increase when RBC count increase and decrease when RBC count decreases (Abidi, 1986). So the increased PVC in the present study could be attributed to increase in RBC count. MCV indicates the average size of red blood cell in a given sample of blood. In the present study the MCV exhibited a significant decrease. Decrease in MCV is generally associated with corresponding increase in RBC, Hb and PCV (Verma *et al*., 1979). Similarly MCH also decreased in the present study. MCHC in the present study showed an increase in pregnant rats due to exposure to teratogenic dose of $CdCl_2$. The increase in Hb in the present study may be the cause for the increase in MCHC.

In the present study a significant increase in WBC count has been noticed. Several authors have noticed similar increase in WBC in animals upon chronic exposure to insecticides (Phillip *et al.,* 1989). Increase in WBC count suggests stepped up defensive capability of rats during $CdCl_2$ stress. Earlier studies also reported mild haematological (Leukopenia) alterations in rats and mice following repeated dose toxicity of N-methyl pyrrolidone, a widely used industrial solvent (Malek *et al*., 1977).

The results clearly showed the prevailing hypoxic conditions in pregnant rats during $CdCl_2$ treatment. The changes noticed in haematological parameters in this study also suggests adaptive capabilities of pregnant rats to changed physiological conditions. It is also evident that, though $CdCl_2$ at teratogenic dose has significant effect on haematological parameters of maternal system, but has no or very little effect on fetal blood parameters.

ACKNOWLEDGEMENTS

Financial support by Council of Scientific and Industrial Research (CSIR) through Research Associateship to ATVR is gratefully acknowledged.

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